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Randomised Controlled Trial
Dental Implants

Does platelet-rich fibrin increase the stability of implants in the posterior of the maxilla? A split-mouth randomized clinical trial

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Abstract. The effect of platelet-rich fibrin (PRF) on bone healing around dental implants in areas of poor bone quality has not been studied. The aim of this study was to evaluate the stability of implants placed in the posterior maxilla, with or without the use of PRF, during the healing period. A split-mouth randomized clinical trial was performed. Twenty patients with missing teeth in the molar region of the maxilla, requiring bilateral implants, were included. PRF was used on one side (group 1); no PRF was used on the other (group 2). Implant stability was assessed by resonance frequency analysis (RFA) at 2, 4, and 6 weeks after placement. At 2 weeks, the mean ISQ was 60.60 ± 3.42 in group 1 and 58.25 ± 3.64 in group 2; at 4 weeks it was 70.30 ± 3.36 in group 1 and 67.15 ± 4.33 in group 2; at 6 weeks it was 78.45 ± 3.36 in group 1 and 76.15 ± 2.94 in group 2. Significant differences in RFA were found between the groups at 2 weeks ($P = 0.04$), 4 weeks ($P = 0.014$), and 6 weeks ($P = 0.027$) after placement. The study results suggest that the use of PRF may enhance the post-insertion stability of dental implants placed in the posterior maxilla during the healing period.

Key words: PRF; implant; stability; bone.

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Dental implants are a standard treatment for the replacement of missing teeth. Stability without micromovement is essential for the osseointegration of implants. Generally, a healing time of 3 to 4 months is required for the osseointegration of dental implants. New implant surfaces can reduce the healing time to 6 to 8 weeks and provide the possibility of immediate loading. Modified implant surfaces can enhance bone-to-implant contact (BIC) and shorten the healing time[1].

Implant stability depends on bone quality. The mechanical properties, degree of mineralization, and remodelling capacity of bone determine the bone quality[2]. Bone quality is classified into four types (types I–IV) based on bone composition, i.e. the

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ratio of compact bone to spongy bone. Compact bone and bone resistance decrease from type I bone to type IV bone[3]. The success rate of implants has been reported to be lower in type IV bone than in the other types[4].

Several techniques to improve the healing of endosseous implants and bone grafts have been suggested[5]. Platelets release growth factors that can enhance cell proliferation and the healing of injured tissues, and these have been used to improve the healing process[6]. Platelet-rich plasma (PRP), a new application of tissue engineering, is an autologous source of various growth factors including transforming growth factor beta (TGF-β), platelet-derived growth factor (PDGF), insulin-like growth factor, and epidermal growth factor. TGF-β and PDGF-AB can improve the healing of soft tissue and bone by increasing collagen production, and can help wound healing and initiate callus formation[7]. Platelet-rich fibrin (PRF) is a second-generation platelet derivative that consists of a fibrin mesh containing leukocytes and cytokines[8]. It has angiogenesis stimulating capacity and releases growth factors such as PDGF[1]. It has been reported that PRF gradually releases autologous growth factors and is more effective for the proliferation and differentiation of osteoblasts than PRP in vivo[7].

Regarding the effect of PRF on bone healing[9], few studies have reported the effect of PRF on implant stability and healing[1,6]. This study was performed to assess whether PRF used in conjunction with implants increases stability. The null hypothesis was that PRF does not promote bone healing around implants or increase stability. The aim of this study was to evaluate the stability of implants in the posterior maxilla during healing following the use or not of PRF at implant placement.

Materials and methods

A split-mouth randomized clinical trial was designed. The sample was derived from the patients of the Oral and Maxillofacial Surgery Department of Shiraz University of Medical Sciences. Patients were recruited from September 1, 2013 to October 31, 2015. The study was approved by the medical ethics committee of the university and has been registered at ClinicalTrials.gov (NCT0234962).

Subjects eligible for study inclusion were partially edentulous with single tooth gaps and free end situations bilaterally and required bilateral dental implants in the first molar area of the maxilla (at least 6 months after extraction). They had to have adequate inter-occlusal and mesiodistal space in the edentulous area, with sufficient bone width and height (at least 5 mm width and 10 mm height). Patients were excluded from study enrolment if they were diabetic or had a disease that affects bone metabolism, had a history of previous bone graft or sinus lift, had used immunosuppressive drugs or corticosteroids, or had a history of radiotherapy or chemotherapy.

PRF preparation

Before starting the surgical procedure, 2 × 10 ml of venous blood was taken and placed in tubes in an IntraSpin centrifuge (Intra-Lock International Inc., Boca Raton, FL, USA). These were centrifuged immediately at 28,000 rpm for 12 min. After centrifugation, the caps were removed from the tubes, and the tubes placed in the sterile rack of the IntraSpin system. The fibrin matrix was then prepared: the leukocyte-PRF (L-PRF) clot was removed from the tube with forceps. The L-PRF was then separated from the red blood cell clot found immediately beneath, and was placed on the surface of the Xpression tray of the IntraSpin system and covered. Five minutes were allowed to pass before the fibrin matrix was removed and used.

Surgical technique

Patients received prophylactic antibiotics (2 g amoxicillin orally) 1 h before surgery. A crestal incision was made on both sides of the maxilla, and the periosteum was elevated using a full-thickness flap to expose the alveolar crest. Using the standard implantation procedure, the site was prepared based on the BEGO implant guidelines (BEGO Implant Systems GmbH & Co. KG, Bremen, Germany): 800 rpm, 20 N.

Randomization was performed using a sealed envelope with a computer-generated random allocation for each patient to determine the side on which the PRF was to be used. On the PRF side (group 1), the fibrin matrix was placed in the implant site immediately before implant placement, and the implant (BEGO, 4.5 mm × 10 mm) was tightened with a hand wrench until primary stability was achieved (25 N). On the non-PRF side (group 2), an implant of the same size was placed without the prior use of PRF. A healing abutment was placed on both sides and the flaps were sutured back in place. Both sides were operated on in one session.

Following surgery, the patients were instructed to apply cold compresses. Medications prescribed for post-surgical use by the patients included analgesics (ibuprofen, 400 mg every 6 h) and an antiseptic oral rinse (0.12% chlorhexidine gluconate mouthwash twice daily) for 1 week.

Implant stability measurements

Two examiners who were blinded to the procedures measured the implant stability. The stability of the implants was assessed by resonance frequency analysis (RFA). The measurements were taken with an Osstell device (Osstell, Gothenburg, Sweden) by connecting the transducer (SmartPeg) to the fixture. The mesiodistal and buccolingual directions were measured and the mean implant stability quotients (ISQs) were calculated. RFA measurements were performed at 2, 4, and 6 weeks after implant placement.

Statistical analysis

The statistical analyses were performed using SPSS version 19 software (SPSS Inc., Chicago, IL, USA). The independent *t*-test was applied to compare ISQ values between the two groups at each measurement time point. *P*-values of <0.05 were considered to be statistically significant. An inter-examiner reliability analysis was performed using the kappa statistic to determine the agreement between the two examiners.

Results

Twenty patients (nine male and 11 female) with bilateral edentulous areas in the first molar region of the maxilla were included in the study. The mean age of the patients was 39.60 ± 6.74 years. Each patient received two implants, one on each side. Group 1 (with PRF) included 20 implants and group 2 (no PRF) also included 20 implants. At 2 weeks after insertion, the mean ISQ was 60.60 ± 3.42 in group 1 and 58.25 ± 3.64 in group 2. There was a statistically significant difference between the two groups ($P = 0.04$). At 4 weeks after insertion, the mean ISQ was 70.30 ± 3.36 in group 1 and 67.15 ± 4.33 in group 2. Analysis of the data demonstrated a significant difference between the two groups at this time point ($P = 0.014$). The mean ISQ was 78.45 ± 3.36 in group 1 and 76.15 ± 2.94 in group 2 at 6 weeks after

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